Single-cell trajectory detection uncovers progression and regulatory coordination in human B cell development.

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Authors: Sean C Bendall, Kara L Davis, El-Ad David Amir, Michelle D Tadmor, Erin F Simonds, Tiffany J Chen, Daniel K Shenfeld, Garry P Nolan, Dana Pe'er

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Public Summary:
Tissue regeneration is an orchestrated progression of cells from an immature state to a mature one, conventionally represented as distinctive cell subsets. A continuum of transitional cell states exists between these discrete stages. We combine the depth of single-cell mass cytometry and an algorithm developed to leverage this continuum by aligning single cells of a given lineage onto a unified trajectory that accurately predicts the developmental path de novo. Applied to human B cell lymphopoiesis, the algorithm (termed Wanderlust) constructed trajectories spanning from hematopoietic stem cells through to naive B cells. This trajectory revealed nascent fractions of B cell progenitors and aligned them with developmentally cued regulatory signaling including IL-7/STAT5 and cellular events such as immunoglobulin rearrangement, highlighting checkpoints across which regulatory signals are rewired paralleling changes in cellular state. This study provides a comprehensive analysis of human B lymphopoiesis, laying a foundation to apply this approach to other tissues and "corrupted" developmental processes including cancer.

Scientific Abstract:
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